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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/576,428

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Martin S. Zand

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06/19/2008

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EXAMINER

SCHWADRON, RONALD B

ART UNIT

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1644

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/576,428	<b>Applicant(s)</b> ZAND ET AL.	
	<b>Examiner</b> Ron Schwadron, Ph.D.	<b>Art Unit</b> 1644	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-56 is/are pending in the application.  
     4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-56 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. ____.                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/28/07 and 4/20/06</u> .                                    | 6) <input type="checkbox"/> Other: ____.                          |

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1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 45-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 45 is indefinite in that it reads on a method of transplantation, yet the last four lines of said claim refer to a method of treating a autoimmune disease. For purposes of prior art, said method, last four lines will be interpreted as referring to the claimed method of transplantation. Claim 49 lacks antecedent basis in claim 46. It should depend from claim 48.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3,9-11,14,16-20,23,25-28,31-37,40,42-45,48,50-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the . . . claimed subject matter", *Vas-Cath, Inc. V. Mahurkar*, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed inventions.

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The claims recite use of antibody variants. The specification does not disclose the identity of any antibody variant. The term variant in the context recited in the claims encompasses a potentially vast array of unknown molecules and mutants of antibodies which are not disclosed in the specification or known in the prior art, wherein said molecules have the functional properties of antibodies. The structure of said molecules is unpredictable. Thus, the written description provided in the specification is not commensurate with the scope of the claimed inventions. In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See *The Regents of the University of California v. Eli Lilly and Company*, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In *University of California v. Eli Lilly and Co.*, 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, *id.* at 1240. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", *Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd.*, 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991). Attention is also directed to the decision of *The Regents of the University of California v. Eli Lilly and Company* (CAFC, July 1997) wherein is stated: The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

Thus, as we have previously held, a cDNA is not defined or described by the

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mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA. See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

5. Regarding the application of prior art, the claimed inventions do not find support in parent application 60/513523 and therefore are not entitled to priority to said application regarding the prior art. There is no support in the parent application for the methods of claims 1/11/20/28/37/45 or composition of claim 53 which recites use of monoclonal antibodies. There is no support in the parent application for the aforementioned claimed inventions that use "polyclonal anti-thymocyte serum". The parent application is limited to the use of thymoglobulin which is defined in the parent application as rATG (see page 20). The term "polyclonal anti-thymocyte serum" encompasses preparations such as those of claims 5/13/22/30/39/47 wherein said preparations are not disclosed in the parent application. There is no support in the parent application for the methods of claims 2/4/6-8 or said limitations as recited in the other methods. There is also no disclosure in the parent application of the use of effective fragments or variants of monoclonal antibodies. There is no disclosure in the parent application of the method of claim 36 which recites all of the diseases recited in said claim. There is no support in the parent application for the method of claim 45.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application

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designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-3,6-8,10,11,14-17,19,20,23-28,31-37,40-44,53-56 rejected under 35 U.S.C. 102(b) as being anticipated by Grewal (US 2002/0197256) as evidenced by Timm et al.

Grewal teaches the claimed composition wherein the antiCD20 and antiCD40 agents are antibodies including the chimeric antiCD20 antibody C2B8(aka RITUXAN or rituximab) or humanized antibodies(see claim 19, sections [0010], [0083]-[0088], [0122], [0133]). RITUXAN causes apoptosis of B cells (see [0010]). The composition could also include two or more different antiCD40 antibodies (see [0128]). Grewal teaches in vivo administration of said antibodies to treat B cell malignancy such as multiple myeloma (see [0107], Table I), wherein RITUXAN causes apoptosis of B cells (see [0010]). Grewal teaches that CD20 occurs on PBL and all B cells until plasma cell differentiation (see [0041], wherein PBL would inherently include CD19+ PBL. The antibodies are administered IV and administration can be repeated (see [0130] and [0126]). The aforementioned antibodies can also be used to treat autoimmune disease such as RA (see claims 21-30). Myeloma cells inherently express CD138 (see Timm et al., se page 1863, second column)

8. Claims 1-4,6,8-10,45,46,48,50,51,53,54,56 are rejected under 35 U.S.C. 102(b) as being anticipated by Bonnefoy-Berard et al.

Bonnefoy-Berard et al. teach treatment of B cells including activated B cells/CD40L activated B cells with rabbit polyclonal anti-thymocyte serum wherein apoptosis is induced (see page 1051, page 1057). The preparation contains antibodies encompassed by those recited in claim 8 (see page 1051, first column) wherein said antibodies are structurally identical to monoclonal antibodies. The rabbit polyclonal anti-thymocyte serum is a composition. Bonnefoy-Berard et al. teach that said composition is used in vivo in organ transplant patients wherein it would inherently have the functional properties recited in the claims. The method of claim 51 encompasses all conventional modes of administration wherein the ALG would have been therefore administered by one of said routes.

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9. Claims 1-4,6,8,10-12,14,16,17,19,20,21,23,25-27,37,38,40,42-46,48,50-54,56 are rejected under 35 U.S.C. 102(b) as being anticipated by Kroger et al. as evidenced by Bonnefoy-Berard et al. and Timm et al.

Kroger et al. teach treatment of myeloma patients with rabbit polyclonal anti-thymocyte serum (see abstract and page 3920). It is an inherent property of said treatment that it causes apoptosis of the myeloma cells in said patients and the cells of claim 2/3 (naturally occurring cells found in humans) because said treatment uses in vivo administration of the same preparation recited in the claims. The preparation inherently contains antibodies encompassed by those recited in claim 8 (see Bonnefoy-Berard page 1051, first column) wherein said antibodies are structurally identical to monoclonal antibodies. The rabbit polyclonal anti-thymocyte serum is a composition. The patients received repeated IV administration of the ATG. The patient received an allogeneic bone marrow transplant (see abstract) wherein the administered rabbit polyclonal anti-thymocyte serum inherently has the functional effects recited in claim 45. Myeloma cells inherently express CD138 (see Timm et al., see page 1863, second column).

10. Claims 1-8,10,45-48,50-54,56 rejected under 35 U.S.C. 102(e) as being anticipate by Sachs (US 2006/0147428) as evidenced by Bonnefoy-Berard et al. Sachs et al. teach a method of transplantation which uses in vivo administration of polyclonal anti-thymocyte serum to humans wherein said antiserum can be derived from pigs or monkeys (see [0249], [0276], [0296], [0304], [0411], [090], and [0304]). It is an inherent property of said treatment that it causes apoptosis of the cells of claim 2/3 (naturally occurring cells found in humans) because said treatment uses in vivo administration of the same preparation recited in the claims. The preparation inherently contains antibodies encompassed by those recited in claim 8 wherein said antibodies are structurally identical to monoclonal antibodies. The polyclonal anti-thymocyte serum is a composition. The patients received repeated IV administration of the ATG. The patient received an organ transplant (see [0116]) wherein the administered polyclonal anti-thymocyte serum inherently has the functional effects recited in claim 45. The preparation inherently contains antibodies encompassed by those recited in claim 8 (see

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Bonnefoy-Berard et al. page 1051, first column) wherein said antibodies are structurally identical to monoclonal antibodies.

11. Claims 1-4,6-8,10,28,29,31,33-36,53,54,56 are rejected under 35 U.S.C. 102(e) as being anticipate by Birck et al. as evidenced by Bonnefoy-Berard et al.

Birck et al. teach a method of treating autoimmune disease including SLE which uses in vivo administration of polyclonal anti-thymocyte serum (ATG) to humans (see claims 30-45, [0042]-[0043]). It is an inherent property of said treatment that it causes apoptosis of the cells of claim 2/3 (naturally occurring cells found in humans) because said treatment uses in vivo administration of the same preparation recited in the claims. The preparation inherently contains antibodies encompassed by those recited in claim 8 wherein said antibodies are structurally identical to monoclonal antibodies. The polyclonal anti-thymocyte serum is a composition. The patients received repeated administration of the ATG. The preparation inherently contains antibodies encompassed by those recited in claim 8 (see Bonnefoy-Berard et al. page 1051, first column) wherein said antibodies are structurally identical to monoclonal antibodies.

12. Claims 1-3,6-8,10,11,14-17,19,20,23-28,31-37,40-45,48-56 are rejected under 35 U.S.C. 102(e) as being anticipate by Hansen et al. (US 2005/0070693) as evidenced by Timm et al.

Hansen et al. teach treatment of autoimmune disease or myeloma or transplant rejection with IV repeated administration of the monoclonal antibodies recited in the claims wherein said antibodies can be humanized and compositions of said antibodies (see claims 53-66, [0003], [0085]-[0090], [0121], [0148], [0153], [0138],[0154]). It is an inherent property of said treatment that it causes apoptosis of the cells of claim 2/3 (naturally occurring cells found in humans) or other cells recited in the claims because said treatment uses in vivo administration of the same preparation recited in the claims to the same patients. Myeloma cells inherently express CD138 (see Timm et al., se page 1863, second column).

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:



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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-6,8-14,16-23,25-27,37-40,42-48,50-54,56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kroger et al. as evidenced by Bonnefoy-Berard et al. in view of Sachs (US 2006/0147428).

Kroger et al. teach treatment of myeloma patients with rabbit polyclonal anti-thymocyte serum (see abstract and page 3920). Said treatment that causes apoptosis of the myeloma cells in said patients and the cells of claim 2/3 (naturally occurring cells found in humans) because said treatment uses in vivo administration of the same preparation recited in the claims. The preparation contains antibodies encompassed by those recited in claim 8 (see Bonnefoy-Berard page 1051, first column) wherein said antibodies are structurally identical to monoclonal antibodies. The rabbit polyclonal anti-thymocyte serum is a composition. The patients received repeated IV administration of the ATG. The patient received an allogeneic bone marrow transplant (see abstract) wherein the administered rabbit polyclonal anti-thymocyte serum inherently has the functional effects recited in claim 45. Myeloma cells express CD138. Kroger et al. do not teach that the myeloma cells are treated in vitro or use of pig or primate ATG. Sachs et al. teach a method of transplantation which uses in vivo administration of polyclonal anti-thymocyte serum to humans wherein said antiserum can be derived from pigs or monkeys (see [0249], [0276], [0296], [0304], [0411], [090],

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and [0304]). The preparation contains antibodies encompassed by those recited in claim 8 wherein said antibodies are structurally identical to monoclonal antibodies. The polyclonal anti-thymocyte serum is a composition. The patients received repeated IV administration of the ATG. The patient received an organ transplant (see [0116]) wherein the administered polyclonal anti-thymocyte serum inherently has the functional effects recited in claim 45. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Kroger et al. teach the claimed method except that the myeloma cells are treated in vitro or use of pig ATG, whilst Sachs et al. teach in vivo methods of treatment which uses in vivo administration of polyclonal anti-thymocyte serum to humans wherein said antiserum can be derived from pigs or monkeys. A routineer would have tested said pig or monkey ATGs in vitro prior to use to assay the properties of said antisera. In KSR Int'l Co. v. Teleflex Inc., 550 U.S. m, 2007 WL 1237837, at "13 (2007) it was stated that **"if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill"**.

15. Claims 1-6,8-10,28-31,33-36,45-48,50-54,56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birck et al. as evidenced by Bonnefoy-Berard et al. in view of Sachs (US 2006/0147428).

Birck et al. teach a method of treating autoimmune disease including SLE which uses in vivo administration of polyclonal anti-thymocyte serum (ATG) to humans (see claims 30-45, [0042]-[0043]). Said treatment causes apoptosis of the cells of claim 2/3 (naturally occurring cells found in humans) because said treatment uses in vivo administration of the same preparation recited in the claims. The preparation contains antibodies encompassed by those recited in claim 8 wherein said antibodies are structurally identical to monoclonal antibodies. The polyclonal anti-thymocyte serum is a composition. The patients received repeated administration of the ATG. The preparation contains

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antibodies encompassed by those recited in claim 8 (see Bonnefoy-Berard et al. page 1051, first column) wherein said antibodies are structurally identical to monoclonal antibodies. Birck et al. do not teach that use of pig or primate ATG. Sachs et al. teach a method of transplantation which uses in vivo administration of polyclonal anti-thymocyte serum to humans wherein said antiserum can be derived from pigs or monkeys (see [0249], [0276], [0296], [0304], [0411], [090], and [0304]). The preparation contains antibodies encompassed by those recited in claim 8 wherein said antibodies are structurally identical to monoclonal antibodies. The polyclonal anti-thymocyte serum is a composition. The patients received repeated IV administration of the ATG. The patient received an organ transplant (see [0116]) wherein the administered polyclonal anti-thymocyte serum inherently has the functional effects recited in claim 45. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Birck et al. teach the claimed method except that the patients are treated with primate pig ATG, whilst Sachs et al. teach in vivo methods of treatment which uses in vivo administration of polyclonal anti-thymocyte serum to humans wherein said antiserum can be derived from pigs or monkeys. In KSR Int'l Co. v. Teleflex Inc., 550 U.S. m, 2007 WL 1237837, at "13 (2007) it was stated that **"if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill"**.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571 272-0841. The fax

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phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ron Schwadron, Ph.D./

Primary Examiner, Art Unit 1644